DETAILED ACTION

This application is a 371 of PCT/US04/040844 filed on 12/6/2004.

Claims 1-12, 15, 22, 28, 48-52 and 54-56 are currently pending.

The preliminary amendment filed on 4/23/2007, canceling claims 13, 14, 16-21, 23-27, 29-47, 53 and 57-95 is acknowledged.

Election/Restriction

Applicant's election with traverse of Group I, claim(s) 1-7, 15, 22, 28 and 48, drawn to a non-mutated or mutated catalytic domain from a galactosyltransferase I or a polypeptide comprising said catalytic domain comprising a conservative mutation at a position corresponds to position 344 of SEQ ID NO: 6 of said domain or polypeptide, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine moiety in the response filed on 8/24/2009 is acknowledged.

The traversal is on the ground(s) that there would be no burden of search for the coexamination of all the Groups in particular Group I and II simultaneously by the examiner. This is not found persuasive because while the search necessary for examination of all the groups may overlap it is not coextensive and searching all the groups together would create a serious search burden to the Examiner. In addition, as discussed previously the shared technical feature of all the groups is that they all relate to polypeptide of SEQ ID NO: 6. However, this shared technical feature is not a “special technical feature” as defined by PCT Rule 13.2 as it does not define a contribution over the art. A galactosyltransferase protein of SEQ ID NO: 6 known in the prior art (Beta-

1,4-galactosyltransferase 1, UniProt Acc. No. P08037, created 8/1/1988), which is 100% identical to SEQ ID NO: 6 of the instant application. In addition, a mutant of bovine beta1,4-galactosyltransferase-1 (met344His) is also known in the art (Boeggeman et al. Glycobiology, 13, Nov 2003, p869, see IDS). Thus, a polypeptide of SEQ ID NO: 6, by default the corresponding nucleic acid molecule and mutant having a mutation at position 344 of SEQ ID NO: 6 or any mutant derived from SEQ ID NO: 6 does not make contribution over the prior art. Thus, all the groups lack unity of inventions. Besides, 37 CFR 1.475 does not provide for multiple products and/or methods within a single application. Therefore, inventions of Group I - VI lack unity of invention. Furthermore, the search is not limited to only patent database but also includes large non-patent databases. Searching Groups I and II and analyzing the vast search results from both patent and non-patent databases imposes a serious burden on the Examiner. Restriction is clearly permissible even among related inventions as defined in MPEP 808, and 35 U.S.C. 121 allows restriction of inventions, which are independent or distinct.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-12, 49-52 and 54-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions.

Claims 1-7, 15, 22, 28 and 48 are under consideration.

Priority

Acknowledgement is made of applicants claim for priority of International

application PCT/US04/040844 filed on 12/6/2004 and domestic priority under 35 USC 119(e) to US provisional application 60/527,615 filed on 12/5/2003.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 5/22/2008 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is considered by the examiner. The signed copy of 1449 is enclosed herewith.

Drawings

Drawings submitted on 6/5/2006 are accepted by the Examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim 48 is indefinite and vague in the recitation of "a polypeptide --- according to claim 43", which is confusing because claim 43 is canceled. It is not clear what the limitation of claim 48 is? The Examiner will interpret claim 48 as dependent from claim 1 for the examination purpose only.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 3-6, 7, 15, 22, 28 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 2, 3-6, 7, 15, 22, 28 and 48 are directed to a non-mutated or mutated catalytic domain from a galactosyltransferase I, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional

characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical*).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.* the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description (see *Enzo* paraphrase above).

Thus, claims 1, 2, 7, 15, 28 and 48 are directed to any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made having any structural feature comprising a conservative amino acid exchange at position 344 and 342 (claims 3-6) corresponding to SEQ ID NO: 6, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium. Claims are thus drawn to any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made having any structural feature comprising a conservative amino acid exchange at position 344 and 342, corresponding to SEQ ID NO: 6 and having the activity of catalyzing the formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium. The specification does not contain any disclosure of the structure of all the mutants, variants or fragments of any catalytic domain of any galactosyltransferase I isolated from any source or man made. The genus of polypeptides as claimed is a large variable genus

including mutants, variants and fragments, which can have wide variety of structures. Therefore, many structurally unrelated polypeptides are encompassed within the scope of the claims. The specification discloses the structure of only a single representative species of the claimed genus (SEQ ID NO: 6) and few mutants, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 2, 3-6, 7, 15, 28 and 48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mutated catalytic domains of a galactosyltransferase I of SEQ ID NO: 6, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium, wherein the mutations are at positions 344, 342, 228 and 229 of a galactosyltransferase I of SEQ ID NO: 6 such as M344H, M344E, M344A, M344S, M344QC342T, R228K and A229G, does not reasonably provide enablement for any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made comprising a conservative amino acid exchange at position 344 and 342 (claims 3-6) corresponding to SEQ ID NO: 6 having any structural feature, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 2, 3-6, 7, 15, 28 and 48 are so broad as to encompass any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made comprising a conservative amino acid exchange at position 344 and 342 (claims 3-6) corresponding to SEQ ID NO: 6 having any structural feature, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to extremely large number of mutants, variants and fragments of any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made comprising a conservative amino acid exchange at position 344 and 342 corresponding to SEQ ID NO: 6 having any structural feature, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only mutated catalytic domains of a galactosyltransferase I of SEQ ID NO:

6, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium, wherein the mutations are at positions 344, 342, 228 and 229 of a galactosyltransferase I of SEQ ID NO: 6 such as M344H, M344E, M344A, M344S, M344QC342T, R228K and A229G.

The art clearly teaches the high level of unpredictability with regard to the effect of structural changes in a protein's activity when no guidance/knowledge as to which amino acids are required for activity has been provided. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. Whisstock et al. (2003) teach that prediction of protein function from sequence and structure is a difficult problem because homologous proteins often have different functions (see abstract). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions. Similarly, at the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. Similarly, Chica et al. (Curr Opin Biotechnol. 2005 Aug;16(4):378-84; PTO 892) teach that the complexity of the structure/function relationship in enzymes has proven to be a factor in limiting the general application of rational enzyme modification and design, where rational enzyme

modification and design requires in-depth understanding of structure/function relationships. The teachings of Whisstock et al. and Chica et al. are further supported by the teachings of Witkowski et al. (1999), where it is shown that even small amino acid changes result in enzymatic activity changes.

The specification does not support the broad scope of the claims which encompass any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made comprising a conservative amino acid exchange at position 344 and 342 corresponding to SEQ ID NO: 6 having any structural feature, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting galactosyltransferase activity; (B) the general tolerance of galactosyltransferase polypeptides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in galactosyltransferase polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made comprising a conservative amino acid exchange at position 344 and 342 corresponding

to SEQ ID NO: 6 having any structural feature, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any mutated catalytic domain from any galactosyltransferase I isolated from any source or man made, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the presence of magnesium is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 7, 15 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Vadaie et al. (Identification and characterization of a Drosophila melanogaster ortholog of human beta1,4-galactosyltransferase VII. Glycobiology. 2002 Oct;12(10):589-97).

The instant claims drawn to any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made having any structural feature, which catalyzes formation of galactose-β(1,4)-N-acetylglucosamine bond in the

presence of magnesium. Broadly interpreting, the claims read on any catalytic domain or a polypeptide of a galactosyltransferase I, which catalyzes transferring galactose to its acceptor molecule in the presence of magnesium

Vadaie et al. teach a galactosyltransferase, which transfers galactose to its acceptor molecule in the presence of manganese, cobalt and magnesium, although the activity is highest in presence of manganese and least in presence of magnesium. (p592, right column, 2nd paragraph). Claim 2 is included in this rejection because "rate of formation of the galactose- β(1,4)-N-acetylglucosamine bond ---- at least two-fold ---- one hundred-fold" in terms of galactosyltransferase activity is an inherent property of the galactosyltransferase enzyme of Vadaie et al. Claim 48 is included in this rejection as interpreting claim 48 depends on claim 1 (see 112 2nd rejection).

Because the galactosyltransferase of the claimed catalytic domain and that of galactosyltransferase of the reference is one and the same as evidenced by Vadaie et al. because Vadaie et al. teach a galactosyltransferase, which transfers galactose to its acceptor molecule in the presence of manganese, cobalt and magnesium, Examiner takes the position that the galactosyltransferase disclosed in the Vadaie et al. reference inherently has "two-fold ---- one hundred-fold" activity as in the claimed catalytic domain. Since the Office does not have the facilities for examining and comparing applicants' galactosyltransferase activity with the galactosyltransferase activity of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed activity of the product and the activity of the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Therefore, Vadaie et al. anticipate claims 1, 2, 7, 15 and 48 of the instant application as written.

Conclusion

Status of the claims:

Claims 1-12, 15, 22, 28, 48-52 and 54-56 are pending.

Claims 8-12, 49-52 and 54-56 are withdrawn.

Claims 1, 2, 3-6, 7, 15, 22, 28 and 48 are rejected.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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